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13. ABSTRACT *(Maximum 200 words)*

Chemotherapy, frequently given to breast cancer patients, destroys lymphocytes as well as cancer cells. It had been observed that the T_H cell ($CD4^+$ lymphocyte) population in the blood is very slow to recover. We observed that in healthy women a resistance exercise program brought about an increase in blood $CD4^+$ T cells. Therefore the goal of this study was to determine if an appropriately designed exercise program would help in the recovery of $CD4^+$ T cells following chemotherapy/radiation. The major accomplishments during this first reporting period are 1) the establishment of a recruitment system; 2) approval by the General Clinician Research Center; 3) the establishment of the functional (mitogen, cytokine) and phenotypic (differentiation and activation markers) assays; 4) the establishment of an exercise protocol and the training of personal trainers. The first subject, enrolled in February of 1998 has now completed 3 months of exercise training. There are 9 subjects enrolled at this time. The data are not complete for any one patient due to the long course of treatment. However, a decrease in lymphocyte function and phenotype following chemotherapy is apparent from the preliminary results.

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Andrew M Martin 6/22/99

PI - Signature Date

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5. INTRODUCTION

Breast cancer patients commonly receive chemotherapy as part of their treatment. Along with the tumor cells, the normal, continually renewing cells of the hematopoietic system are targets for the cytotoxic drugs. Hematopoietic stimulating factors can correct certain other blood cell populations but loss of blood lymphocytes remains uncorrected. One population of lymphocytes, $CD4^+$ T cells (T helper cells), a major regulator of the immune system is particularly susceptible to chemotherapy-induced depletion. $CD4^+$ T cell levels in the blood may fall to those seen in AIDS patients (Kilmas et al. 1991) and remain low for many months after chemotherapy ceases (Hakim et al. 1996). Nevertheless we have measured an increase in $CD4^+$ T cell levels in normal healthy females after 3 months of resistance exercise training. There are similar reports of increases in $CD4^+$ T cells in HIV seropositive individuals following training (La Pierre et al. 1991). Therefore, we hypothesized that an appropriately designed exercise training program will help in the recovery of $CD4^+$ T lymphocyte levels following chemotherapy. We have proposed to determine the total numbers of $CD4^+$ T lymphocytes in the blood before and after chemotherapy/radiation and after three and six months of exercise training. We plan to determine underlying cellular mechanism by assaying lymphocyte populations especially $CD4^+$ T cells, subpopulation differentiation, activation, and apoptosis and to demonstrate that the exercise program designed for the individuals is sufficient to improve physical fitness, quality of life and to decrease fatigue (Mock et al. 1994).

6. BODY: RESEARCH ACCOMPLISHMENTS ASSOCIATED WITH TASKS

Task 1: PROCEDURES TO COORDINATE WITH CLINICIANS AND CANCER PROGRAM COORDINATOR

a. Physicians

Upon notification of the award the PI (Andrea Mastro) and CoI (William Kraemer) met with the two local physicians and the Centre Community Cancer Coordinator who are associate investigators: Dr. Aron Bleznak, Surgeon; Dr. Richard Dixon, Oncologist; and Judy Underwood, RN and Coordinator of the Centre Community Hospital Cancer Center. We discussed recruitment goals and procedures, consent forms, staff contacts in each office and anticipated issues.

We designed a brochure (appended) which was placed in local physicians' offices, (oncologist, general pratictioners, ob/gyn, etc), in various areas of the hospital and in the office of the local chapter of the American Cancer Society.

We also developed standard forms for physician consent and an information sheet for staff in the clinicians offices (appended). We met with the office staff including the individuals who administer the chemotherapy in order to familiarize them with the study and the procedures.

Dr. Nancy Williams (CoI) and Dr. Mastro made an hour long presentation to the Cancer Group Meeting of the Centre County Community Hospital in October of 1998. This meeting includes all of the local clinicians who deal with cancer patients as well as nurses and support staff. We discussed the immunology as well as demonstrated some of the exercises.

We continue to be in weekly contact with the physicians by email or phone and in person when needed. At this point the procedures for recruiting in the Centre County Area are well in place. Nevertheless, we are constantly looking for ways to make the study known. For example, the study will be the subject of an article in the "Living section" of an upcoming issue of the local newspaper, the Centre Daily Times. Following publication, we will place general ads in the newspaper which serves the Central Pennsylvania area. In addition, the public relations office of the University has agreed to help us gain more publicity.

b. Approval by General Clinical Research Center

The General Clinical Research Center (GCRC) of the Pennsylvania State University at University Park is supported by a grant from the National Center for Research Resources of the National Institutes of Health and by the Penn State Milton S. Hershey Medical Center, College of Medicine and the Noll Physiological Research Center (appended). We were invited to submit our protocol for this study to the GCRC and were approved by them in May of 1998. As an approved study the GCRC provides various services: the nursing staff draws blood and arranges CBCs, and aids in the administration of physical exams at the time of the fitness evaluation; the physician, Dr. Ann Trout, M.D., administers physical exams and takes part in the fitness evaluation; the exercise physiologist, Jan Depp M.S., administers the tests for VO_2 Max and for muscle-function; the cytokine core facility will test for secreted cytokines and aid in the detection of intracellular cytokines; the dietician, Judy True, M.S., R.D. has aided in the development of an appropriate diet survey and will advise in the summation of the data; and the biostatistician and an Assistant Professor of Statistics, Dr. Mosuk Chow, advises us with data collection and will help with the final data analysis.

Task 2: RECRUITMENT OF SUBJECTS

Recruitment depends on the diagnoses of women with breast cancer and thus can not be done at one time but is a continual process. We have put in place channels for recruitment mainly at the local hospital which deals with patients from the Central Pennsylvania area. In addition, we are now working with the Penn State Hershey Medical Center which is about 100 miles away from the University Park Campus, to recruit 1) Centre County residents who travel to Hershey for their treatment and 2) individuals from the more Eastern part of the state who will serve as controls, i.e. "no exercise". As described under Task 1, we also have planned more publicity.

Task 3: MEET WITH POTENTIAL SUBJECTS AND OBTAIN BASELINE VALUES

Drs. Bleznak, Dixon and Nurse Judy Underwood meet nearly every women being treated for breast cancer in the Centre County area. If the woman is to receive chemotherapy, the study is explained to her briefly by one of these individuals or by his/her staff. With the patient's consent, Dr. Mastro or Dr. Williams arranges to meet with them and explain the study in more detail. The potential subject is provided with the informed consent prior to the meeting so that she has time to read it. At the meeting Dr. Mastro or Williams answers questions and the

informed consent is signed. At this time the subject is given the first set of questionnaires and a blood draw is taken.

One problem that has come up a couple of times is that the woman was given information about the study at the same time that she learned that she was to receive chemotherapy. She was very emotionally distraught and did not wish to discuss the study. However, once she had time think over the situation she asked to join the study. We decided that obtaining a post-chemotherapy/ post-radiation value for $CD4^+$ T cells would give the nadir value. Since the results are being compared within one subject we will be able to follow recovery of $CD4^+$ T levels from the end of chemotherapy through radiation and the six month exercise period. Therefore we will admit subjects into the study at his point.

The GCRC has a nursing staff that draws blood and arrange to have a CBC done. Sometimes blood is obtained from the hospital laboratory in order to avoid the subject having to give blood more than necessary. The blood is brought back to our own laboratory for further analyses.

Task 4: PROTOCOLS FOR IMMUNOLOGICAL, BIOCHEMICAL, FLOW CYTOMETRIC AND CELLS ASSAYS.

Dr. Mastro worked with Sue Messics to establish and test the protocols. Sue Messics was hired in January of 1999 to carry out the immunological assays. She came with 13 years training as a research technologist. She had taken courses in flow cytometry from Becton Dickinson as well as a course in flow cytometry at the Los Alamos Laboratories in New Mexico. She is well suited to work on this aspect of the project.

We determined that the following protocols were optimal for the study:

a. Whole blood mitogen assays

This procedure (Bloemena et al. 1989) is used to determine the extent of cell activation in response to 3 polyclonal mitogens phytohemagglutinin (PHA), concanavalin A (Con A) and pokeweed mitogen (PWM). Blood is collected in lithium or sodium heparin tubes and kept at room temperature until used. Blood is diluted 10 fold (1 ml blood plus 9 ml PBS) with phosphate buffered saline (PBS). One hundred microliters of diluted blood is added to round bottom, 96 well plates. The plates contain mitogens, 100 µl per well so that the final concentration of mitogen is 200 µl as follows PHA: 5, 10, and 50 µg/ml; ConA 3, 12, 25 and 50 µg/ul; and PWM 0.25, 2.5 and 5.0 µg/ml. Six wells of each mitogen at each concentration are used. Six wells of cells with no mitogens serve as baseline controls.

The cells are incubated (37°, 95% air –5% CO) in a humidified incubator for 72 hours. For the last 6 hours, ^{3}H-Thymidine (6.7 Ci/mM) is added at 1 µ Ci/well. At the end of this pulse the lymphocytes are harvested onto glass fiber filters. The radioactive incorporation, CPM, is detected using a ß-plate counter. The data are collected, the replicates averaged and the standard deviations calculated. The average values are plotted vs concentration of mitogen to determine maximal concentrations. The value at each concentration of each mitogen will be compared as will the concentration of maximal response for each mitogen. Values will be compared for each

subject over time. Dr. Mosuk Chow, Assistant Professor of Statistics and the Biostatistician of the GCRC at the Penn State University has advised that repeated measurements on the same individual be analyzed by the Proc Mixed Program in SAS.

b. Whole blood phenotyping

This procedure is used to enumerate the proportions of lymphocytes in whole blood that bear specific surface antigens which indicate cell type, function, and activation state. A Becton-Dickinson flow cytometry consultant spent several days with us advising us on the most recent procedures for analyzing human blood (Mandy et al. 1997).

Blood is collected in lithium or sodium heparin and kept at room temperature. Blood (500 µl) is diluted with PBS (Ca^+, Mg^+- free) 500 µl. Backpipetting is used in order to be as accurate as possible.

The panel of antibodies (Table 1 appendix) was chosen to determine the basic concentration of $CD4^+$ lymphocytes as well to describe their status, e.g. CD45RA identifies naive cells. The antibodies (5 µl) are added to (12X75) tubes followed by addition of 100 µl of the diluted blood. The tubes are vortexed and refrigerated for 20 min before the red cells are lyzed with a hypotonic buffer (ACK). The lymphocytes are washed by centrifugation and resuspension in PBS, and fixed with 1% formaldehyde before being analyzed by flow cytometry.

We modified this procedure from the one originally proposed by using an LCA, CD45 conjugated with ECD. ECD does not interfere with the FITC or PE conjugated fluorochomes of the other antibodies. This antibody is added to every sample. Because LCA labels only leukocytes it is used to set an internal gate in each sample. When combined with forward and side scatter it is used to gate only lymphocytes.

The panel (Table 1) was modified slightly from that originally proposed to include CD45-ECD in every sample. The antibody to CD45 recognizes all leukocytes. When combined with the physical properties of the cells it allows gating on the lymphocyte population.

We also added an isotype control and the combination of CD4/CD8 in the same sample. The latter serves as an internal control for compensation since the two subpopulations, $CD4^+$ and $CD8^+$ cells should be mutually exclusive in peripheral blood.

We originally standardized a panel using normal blood. We now realize the blood from individuals with cancer or following chemotherapy and radiation are not normal and may not give the expected patterns (Fei et al 1993). We are now including in the panel a Simultest CD3/CD19 reagent tube (Becton Dickinson) as well as the CD4/CD8 tube to establish gates. We also plan to run a CD Chex Plus™ control. CD Chex Plus™ (Streck Labs) is a stabilized preparation of normal human periperial blood leukocytes to be used as a control when evaluating monoclonal antibody binding by flow cytometry. The kit included lot-specific ranges for common surface markers such as CD3, CD4 and CD8.

In order to determine total T $CD4^+$ we currently add Coulter Flow-Count™ Fluorospheres to a tube containing anti CD4 antibody and one to containing anti CD3. We have obtained samples of Becton-Dickinson "True Counts™" and will compare the results with the Flow-Count™.

Apotosis Assays

1) Annexin V

In order to determine the extent of apoptotic cell death in the blood at the time of assays we have tried three assays. Isolated lymphocytes are incubated with fluorescently labeled Annexin V, a protein that binds to the surface of apoptotic cells, and changes the integrity of the membrane to allow propidium iodide (PI) to enter (Vermes et al. 1995). These apoptotic cells are identified as Annexin V^+ and PI^+ by flow cytometric analysis. As a positive control we also treat lymphocytes with radiation or campothecin. We found that with human peripheral blood lymphocytes that annexin staining is visible by flow cytometric analysis but it is not very bright.

2) APO 2.7

In order to increase the sensitivity of the assay for apoptotic cells we tested the use of APO 2.7 as a detection antibody (Roth et al. 1996). This antibody recognizes a 38 Kda mitochondrial membrane protein which is exposed on cells undergoing programmed cell death. This protein appears to be involved in a molecular cascade of apoptosis rather than as a product of cell death.

To establish the technique in the laboratory we used Jurkat cells, a human T cell line, induced with anti Fas (CD95) antibody. This treatment leads to apoptosis (appendix Fig. 1). We plan to use the APO 2.7 technique whenever possible. We will use JURKAT cells treated with Fas ligand as a positive control for each sample.

3) Propidium Iodide and Cell Cycle Analysis

A sample of whole blood is fixed with an equal volume of 70% ETOH. The cells are washed, resuspended in PBS and stained with propidium iodide. Under these conditions PI stains the DNA of all of the cells. Apoptotic cells are recognized by a DNA content of less than 1C. This approach is quicker and easier than 1 and 2 and requires less blood. However, it is less sensitive. When blood volume is a limitation it will be used.

d. Cytokine Assays

Cytokine production by activated lymphocytes provides a good assessment of functionality of the cells. The particular panel of cytokines produced indicates the functional subgroup to which the cells belong; e.g. T_H1 (IFNγ, IL-2) vs T_H2 (IL-4, IL-10).

In one approach whole blood diluted as per the mitogen assay is incubated with a T cell mitogen PHA at 10 μg/ml for 48 hr. The cells are cultured in 2 mls of medium. Control cultures have no mitogen added. After 48 hr the cells are collected and centrifuged. The culture medium is collected, aliquoted and frozen. The CGRC cytokine core facility will assay these for cytokines using established ELISA techniques. All samples from one subject will be assayed at one time following the last sample collection point. We will assay for IFNγ and IL-4 as indicators of T_H1 and T_H2 cells respectively.

In order to determine which cytokines are being made by individual T lymphocytes we plan to use an intracellular cytokine assay (Maino and Picker, 1998). In this approach antibodies to the

cell surface are used to identify all subtypes, i.e. CD4, CD8, while antibodies to the cell cytoplasm are used to detect cytokines in permeabilized cells. The antibodies are directly conjugated to different fluorochromes so that flow cytometric analysis can be used to identify cells that bind both antibodies, i.e. $CD4^+$ and $cytokine^+$. Because this technique is not yet fully established we are freezing samples of blood for later analysis. We know from discussions with an individual at the CDC that frozen, isolated blood lymphocytes can be recovered and activated for intracellular cytokine assays.

Task 5: EXERCISE PROGRAM

Acquaint personnel with specifics of the exercise program (e.g. exercise techniques, exercise prescriptions procedures) and pilot test all procedures for exercise testing and training.

Dr. Nancy Williams, Assistant Professor of Kinesiology has joined the study as a co-investigator and is directing the exercise program.

Dr. Williams arranged for Mr. Richard Hartzell, President and founder of the "Jumpstretch, Inc" to visit Penn State and to demonstrate the use of the Flex Bands®. These bands are used to provide resistance exercise without the need for weights. They are readily adaptable to individuals with specialized needs, i.e. muscle injury following mastectomy, fragility etc. Mr. Hartzell provided video tapes as well as a live demonstration. The program was attended by the PI, CoI and by the graduate student/trainers.

A set of Flex Bands® was purchased for each subject so that she will be able to carry out the home part of the program without the need to buy weights or other specialized equipment or to attend a public gym.

Following the demonstration Dr. Williams and the trainers developed an exercise protocol (appended) and schedule. Mr. Jim Marx, DVM, Ph.D. candidate Kinesiology, was appointed coordinator. A Kinesiology student, Sheri Foura, who also is an experienced trainer was hired to begin the exercise program. Miss Foura will earn a BS in Kinesiology from Penn State in August of 1999. She has worked as a trainer on two other large studies. She is also an Emergency Medical Technician and certified in CPR. She has worked as a personal trainer for a fitness center and has instructed at National Cheerleading camps. We plan to hire more trainers as needed.

Dr. Williams coordinated with the GCRC Exercise Physiologist to establish the protocols for physical fitness evaluation (appended).

The exercise evaluation and exercise training was piloted with Dr. Mastro as the subject.

Dr. Williams also invited an experienced personal trainer from Pittsburgh, Paula M. Franitti, MS to meet with the group of student trainers. Ms. Franitti is a trained exercise physiologist who has her own business "Reformation Ventures." She has extensive experience in working with individuals who are rehabilitating from an injury, sickness, etc. She discussed not only how to work with them physically but how to encourage them to continue in the program.

Dr. Williams and Mastro along with the exercise coordinator, Sue Messics, the laboratory coordinator and the personal trainers meet weekly to discuss the projects and the status of the subjects.

Task 6: ENROLLMENT OF SUBJECTS

Thus far nine women have been enrolled into the exercise groups. They range in age from 38-65 years. Due to the long course of chemotherapy/radiation the first subject enrolled is currently into month 2 of the 3 months of supervised exercise training. Five other women have undergone exercise evaluation and are beginning the supervised training. Because enrollment is limited to breast cancer patients who can take part in an exercise program we are limited in recruitment techniques. However, as described under task 1, we plan to recruit control subjects from another campus and to increase awareness of the study locally.

Task 7: SELECTION OF QUESTIONNAIRES

We also finalized the questionnaires to assess quality of life, diet, and activity. The quality of life questionnaire was submitted at the time of the original proposal. It is "Functional Assessment of Cancer Therapy-Anemia (Fact An) Questionnaire" by Yellen et al, 1997 (appended).

Dr. Judy True, M.S., R.D., dietician of the GCRC has helped us adapt a food frequency form from the Nutritionist Five Program, First Data Bank of San Bruno, Ca. (appended). Dr. Williams selected the Paffenbarger Physical Activity Questionnaire (Paffenbarger et al. 1978) (appended).

Tasks 8-13:

These tasks are repeated task for each individual, i.e. recruit, initial blood analyses ($CD4^+$) and questionnaires, follow up questionnaires during and following chemotherapy and throughout exercise, blood samples following chemotherapy and exercise etc.

We present data from one subject (JM0398) as an example. This subject is a 61 yr old individual diagnosed with ductal adinocarcinoma. She was treated with four cycles of Cytoxan and Adriomycin followed by Tamoxifen. She underwent radiation therapy for approximately six weeks.

The mitogen assays indicates that regardless of the 3 mitogens tested, PHA, ConA or PWM, there was a greater than 63% decline in DNA synthesis of her cells following chemotherapy (Fig 2). Following radiation the decline was greater than 86%. If the CPM were compare for maximal dose of mitogen the responses were even poorer. As expected the T cells (PHA,ConA) as well as B cells (PWM) gave are very poor responses to polyclonal activators. The cultures were adjusted for cell numbers and the percentage cells were not very different (Fig 2). Thus there is an inherant inability of these cells to respond.

The phenotyping (Fig 3) indicated that following chemotherapy the percentage of $CD4^+$ T cells was about 86% of that prechemotherapy. However, the total $CD4^+$ T cells/ul was only 44%. After radiation the percentage was 66% of the prechemotherapy values, the total $CD4^+$ T cells was only 14%. Again as predicted the $CD4^+$ levels were greatly reduced. This subject has just begun training. We will repeat these measurements in three months.

7. KEY RESEARCH ACCOMPLISHMENTS

- the establishment of a recruitment system
- approval by the General Clinician Research Center
- the establishment of the functional (mitogen, cytokine) and phenotypic (differentiation and activation markers) assays
- the establishment of an exercise protocol and the training of personal trainers

8. REPORTABLE OUTCOMES

Because of the length of time from subject recruitment until the exercise program begins we do not yet have one complete data set for a subject. Our study is still in the beginning stages and all the data are preliminary. Therefore, we have no manuscripts, abstracts or presentations to report at this time.

The students who are serving as trainers consider this an excellent project to gain experience for future work.

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10. CONCLUSIONS

A resistance exercise program has been designed to test the hypothesis that exercise training can aid in the recovery of lymphocyte subpopulations especially $CD4^+$ T cells following chemotherapy from breast cancer. Assays to determine the changes in blood cell phenotypes, functions and activation status have been established in the laboratory. A recruitment program has been put in place. Women who have been diagnosed with breast cancer and who have received chemotherapy have entered the program. A decrease in their blood lymphocyte subpopulations as well as cell division in response to polyclonal mitogens in vitro is greatly reduced. However, at this time the data are incomplete, as no subjects have yet completed the exercise training program. Should this program prove beneficial, it will provide a non-invasive therapy that should help in the recovery of a healthy immune system and also in a feeling of general well being.

11. APPENDIX

1. Recruitment brochure
2. Physician Consent form
3. Staff information form
4. GCRC information
5. Table 1.
6. Figures 1-3
7. Exercise protocols
8. Physical Evaluation Protocols
9. Quality of Life Questionnaire
10. Diet Report
11. Physical Activity Report

MASTRO

DAMD 17-98-1-8142

Penn State

Exercise Program For Breast Cancer Patients

***Physical activity and breast cancer**

Recently much attention has been directed toward the potential **benefits of physical activity in preventing breast cancer *and* in accelerating the recovery of the immune system** of breast cancer patients who have undergone chemotherapy. In addition, other benefits of regular physical activity include:

Improved:	***Decreases in:***
•Aerobic fitness	•Depression
•Body composition	•The risk of developing cardiovascular and metabolic disease.
•Muscle strength	
•Balance	
•Self esteem	
•Body image	

***Exercise and Immune Function Project**

Researchers at Penn State University and local physicians are seeking participants for a research project to determine whether regular exercise can help in the recovery of a certain class of white blood cells (T lymphocytes) following chemotherapy for breast cancer. These white blood cells are important in the response of the body to fight off bacteria, viruses and tumor cells. One side effect of chemotherapy is often decrease in number of these cells. The researchers believe that a specialized exercise training program may stimulate an increase the numbers of these cells and therefore aid in the restoration of good health.

To be eligible to participate you must:

* be diagnosed with breast cancer
* be between the ages of 25 and 80
* have your physician's consent to be in the program
* be able to carry out normal daily activities
* have undergone or will undergo chemotherapy

About the exercise program:

The exercise will be of light or moderate intensity, a combination of strength building and aerobic exercise. All exercises will be adapted to the participant's initial fitness level and easily adapted for the home.

Participants will be randomly assigned to either light or moderate exercise groups, and then will train 3 times per week with a personal trainer for 3 months in a small class with other participants. For the next 3 months, participants will be asked to continue to exercise regularly on their own at home, while maintaining records of their exercise and regularly checking in with study personnel.

In order to measure the effect of the exercise on white blood cells, blood samples will be collected 4-5 times over the course of the study; before and after chemotherapy, and at the beginning, middle, and end of the exercise training.

Participants will also be asked to periodically fill out a questionnaire about their perceived quality of life, their nutritional habits, and their physical activity

Participant Benefits:

* Free personalized exercise program
* Information about your fitness and body composition
* Information about the status of cells of your immune system
* Possible improvements in the rate of recovery of immune cells after chemotherapy

Signing up for the project:

If you are interested, fill out the other side of this pamphlet and return it to the nurse in your doctor's office. You will be contacted by either Dr. Andrea Mastro (814-863-0152) or Dr. Nancy I. Williams (814-865-1346), who will explain the program in more detail. You may also contact them directly.

Penn State Exercise Program For Breast Cancer Patients

Name _____

Address _____

Phone _____ Email _____

Referring Physician _____

Physician Phone Number _____

Please check whichever of the following are appropriate:

___ I will begin chemotherapy shortly, within ____ weeks

___ I have already been undergoing chemotheraphy for ____ weeks

MASTRO
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PHYSICIAN'S CONSENT

BREAST CANCER AND EXERCISE STUDY

I_____(physician) give permission

for my patient _____ to take part in the Breast Cancer and Exercise Study. She has no significant physical limitations or other pathologic conditions to prevent her from carrying out her daily functions .

Physician's signature_____

Date_____

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TO: Nursing Staff in the Office of Drs. Dixon and Walker

FROM: Andrea Mastro, Professor of Microbiology and Cell Biology, Penn State

RE: Project " **The Use of Exercise to Increase CD4+ T Lymphocytes following chemotherapy from Breast Cancer"**

Investigators: Andrea Mastro and William Kraemer (Penn State); Richard Dixon (IMA), Aaron Bleznak (Geisinger), and Judy Underwood (Centre Community)

We have previously talked with some of you about this project which is now going to be funded by the Army Breast Cancer Program. We would like your help in recruiting patients but we do not want to add to your already busy workload. Would you be willing to inform likely candidates about the study and ask if we may contact them? I will supply copies of two short flyers, one which gives an overview of the study for your information and also one to be handed out to patients.

Either Dr. Kraemer or I will then contact the patients and meet with them to explain the study and obtain written consent. If they do enter the study we will need to keep track of their treatment so that we can determine when to obtain blood samples and when to begin the exercise testing. We will provide a form that can be kept in the patient's file. We can contact the office about once a month and ask you to fax us the updated form.

For each patient we also will need a letter of consent from the physician. We will provide a form letter for this purpose. We also are providing copies of questionnaires to be filled in by the patients at the initial blood collections in your office.

We appreciate your cooperation and any suggetions for making the process as smooth as possible and the information as clear as possible for the patients. Thank you.

STAFF1

Publication Credit

For purposes of continued support of the Center, we request that you document the GCRC contributions in all publications using any of the GCRC resources. Manuscripts for publication should include a statement similar to the following "The nursing care provided by the staff of the Penn State General Clinical Research Center at the Noll Physiological Research Laboratory is appreciated. The study was supported by NIH Grant M01-RR-10732." Copies of all published manuscripts, articles, or abstracts documenting research on the GCRC should be sent to the administrative coordinator.

CAP, MCAP, CLINICAL SCHOLAR Programs

Guidelines and application kits for these programs are available from the Office of Research Affairs (C1614) at the Hershey Medical Center. Questions regarding eligibility for these programs may be referred to Ernest Johnson, Ph.D. at (717) 531-8495 or Lawrence Sinoway, MD at (717) 531-6853.

For further information, to arrange for a tour of the Center or to apply for use of the GCRC, please call on us:

General Clinical Research Center
Pennsylvania State University
Noll Physiological Research Laboratory
University Park, Pennsylvania 16802-6901

Phone: (814) 865-7103
Fax: (814) 865-0351
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Lawrence Sinoway, M.D. (717) 531-6853

Medical Director
Lars Larsson, M.D., Ph.D. 865-3453

Research Director; Director, Muscle Core Lab.
John Kirwan, Ph.D. 863-0724

Director, Cytokine Core Lab
Joseph Cannon, Ph.D. 865-3453

Nursing Coordinator
April White, R.N., B.S. 863-3182

Biostatistician
Janice Derr, Ph.D. 865-3541

Dietitian
Judy Treu, M.S. R.D. 865-0367

Administrative Coordinator
Rebecca Jenkins, MPA (717) 531-5619

PENN STATE GENERAL CLINICAL RESEARCH CENTER

General Clinical Research Center (GCRC) of The Pennsylvania State University at University Park

The GCRC is supported by a grant from the National Center for Research Resources of the National Institutes of Health and by the Penn State Milton. S. Hershey Medical Center College of Medicine and the Noll Physiological Research Center. The GCRC provides personnel support and facilities for investigator initiated peer-reviewed research with human subjects. The objectives of the GCRC are to facilitate the transfer of basic medical knowledge to the clinical arena, to elucidate pathogenic mechanisms of disease, and to develop strategies for health promotion and disease prevention.

The GCRC provides the expert support personnel that are necessary to perform quality clinical research studies, outpatient procedure and testing rooms, a metabolic kitchen, supplies and equipment. Support personnel include nurses, a dietitian, diet technicians, a computer systems manager and biostatistician. Since 1994, over 20 different protocols have utilized the GCRC facilities. The GCRC supports investigators funded by NIH and other federal, state and local agencies as well as by the private sector. The GCRC also makes space and support services available for faculty to conduct research initiated and sponsored by pharmaceutical or other biomedical industries. The terms of the grant require that we recover all costs of supporting pharmaceutical and industry initiated research.

To initiate a study, contact the Nurse Coordinator (April White at 863-3182) for information and application instructions. The Research Director (John Kirwan at 863-0724) is available to meet with investigators to discuss the use and resources of the GCRC. An Advisory Committee, appointed by the dean, reviews all protocols submitted for GCRC use. Protocols are reviewed for scientific merit and for need of GCRC services. The Advisory Committee sets priorities and policies for the GCRC. Protocols must be approved by the Institutional Review Board (IRB).

Special grants for new investigators are available only through an NIH funded GCRC. The funding of the GCRC by NIH allows Penn State to participate in the Clinical Associate Physician (CAP), Minority Clinical Associate Physician (MCAP) and Clinical Research Scholars (CRS) programs. These grants offer unique opportunities for young investigators.

For investigator-initiated, peer-reviewed studies carried out in the GCRC, the following resources are available at no cost to the investigators.

Nursing

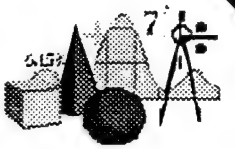
A staff of registered nurses and medical assistants, experienced in the implementation of clinical research studies, is available. Outpatient services are offered Monday-Friday from 7:30 AM to 4:00 PM. Evening and weekend hours are available on request. The GCRC staff functions as a team, working with other health care professionals to optimize and facilitate the research studies. The clinical nurses' skills include intravenous therapy, venipuncture, frequent blood sampling, administrating investigational drugs, managing pharmacokinetic studies and complex specimen handling and processing. The nursing staff co-ordinate and implement screening of subjects for medical clearance into studies. They also initiate and maintain confidential medical records on all subjects.

Nutrition Services

A research dietitian, diet technicians and a metabolic kitchen can provide investigators with nutrition services to plan and prepare weighed metabolic, or constant diets for studies. The research dietitian is available for nutrition counseling and analysis of food records. Specialized meals are available as needed on a daily basis and meals are available to be packed out. The GCRC Nutrition staff maintains a close working relationship with other services of the GCRC, supervises nutrition related research and can provide specialized training in the area of nutritional research.

Computer Services

The Computerized Services Database Management and Analysis System contains computer hardware and software for data management and analysis. Software packages include Excel, SAS, Powerpoint and Access. Data are copied nightly ensuring the highest standards of data management.



Biostatistics

The GCRC biostatistician is available to help investigators with study design, sample size and power estimations, data analysis and related issues. Investigators are encouraged to meet with the biostatistician before submitting a protocol to the Advisory Committee.

Ancillaries

The GCRC has limited funds available for routine and specialized laboratory tests performed at the Noll Laboratory, in the Core Endocrine Laboratory and to be sent to appropriate outside laboratories. The GCRC can help facilitate the selection of laboratory tests for use in study protocols. Other ancillary procedures, such as X-rays and ECG, can also be arranged.

Core Laboratory Services

The GCRC core laboratory provides specimen processing services and provides specialized assays required by more than one investigator. The Muscle Core provides a range of services for the analysis of human muscle samples including: histochemical determination of muscle fiber type, fiber area and capillary density; biochemical determination of muscle enzyme activity and muscle substrate levels. The Cytokine Core has the capability of assaying blood and tissue specimens. ELISAs are used to measure IL-1β, IL-6 and TNF in biological fluids.

Clinical Resources and Equipment

The following is a partial list of equipment available in the GCRC: IVAC infusion pumps, refrigerated centrifuge, twelve lead ECG machine, code blue resuscitation cart, glucose analyzer, hematology analyzer. Arrangements can be made for access to physiological equipment in the Noll Laboratory including: oxygen & carbon dioxide analyzers, hydrostatic weighing equipment, bioelectrical impedance instrumentation and whole body calorimetry.

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Table 1: Monoclonal Antibodies used to identify Lymphocyte subpopulations

Antibody combination	Cells recognized	Significance
CD45-ECD[a]	Leukocytes/monocytes	Used together with forward and side scatter to gate an exclusively lymphocyte population
FITC / PE Ig-G1-/IgG2a-	none	Isotype control
CD4/CD8	T_h (CD4), T_c (CD8)	Two T cell populations; should be mutually exclusive
CD3/CD4	Total T cells (CD3)/T_h (CD4)	Total T cells and percentage that are T_4
CD45RA/CD4	Naive T/T_H (CD4)	Determination of whether CD4 cells are from the thymus ($CD45RA^+$) or from peripheral stores ($CD45RA^-$)
HLADR/CD4	Activated cells/CD_4	Indicates whether CD4 cells are activated, memory cells
CD4/CD69	CD4 T cells/nuclear activation	Indicates whether the CD4 cells are in the process of cell division
CD57/CD8	Suppressor lymphs/ T_c (CD8)	Indicates the number of suppressor lymphs able to down regulate the CD4 lymphs
CD19/CD16	B cells/NK	Indicates the identity of non-T-lymphs
CD3/ CD 16 + CD56	Total T/total NK	Indicates the $Cd3^-$ NK population
CD4+beads [b]	Th (CD4)	Absolute count of $CD4^+$ cells
CD3+beads [b]	T_{total} (CD4)	Absolute count of $CD3^+$ cells

[a] added to every sample to allow gating with each sample

[b] This sample is prepared with precise volumes; addition of volumetric spheres (Flow-Count™ fluorospheres) at a known concentration are counted simultaneously with the lymphocytes during flow cytometry.

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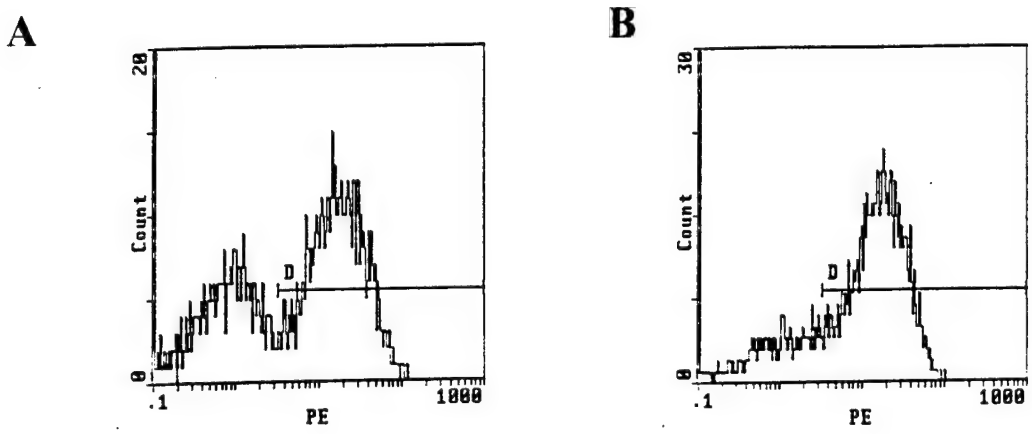

Figure1. Detection of Apoptic Cells with APO 2.7.

Jurkat cells were plated at 10^6 cells in 2ml of RPMI 1640 medium with 10% FBS in glass,d siliconized 12x75 mm tubes. Fas ligand (300 ng/ml) was added and the cells incubated for 6 hours. The cells were centrifuged (200 x g, 7 min) and the culture medium removed. Ice cold digitonin (100 ul of 100 ug/ml) was added to permeabilize the cells. The tubes were incubated on ice for 20 min; 2 ml cold PBS containing 2.5% FBS, 0.01% NaN_3 (PBSF) was added. The cells were centrifuged and the supernatant removed. Apo 2.7 (20 ul, Immunotech, Inc) was added to the cell pellet along with 100 ul of PBS. After the tubes were incubated in the dark for 10 min at room temperature, 2 ml of cold PBSF was added, and the cells centrifuged and the supernatant removed. PBSF (0.5ml) was added and the cells held on ice until analysis with the flow cytometer.

Shown are A, the "control" cells, cultures which had reach saturation, 50.1% apoptotic; and B, the same cells treated with Fas ligand, 59.2% apoptotic

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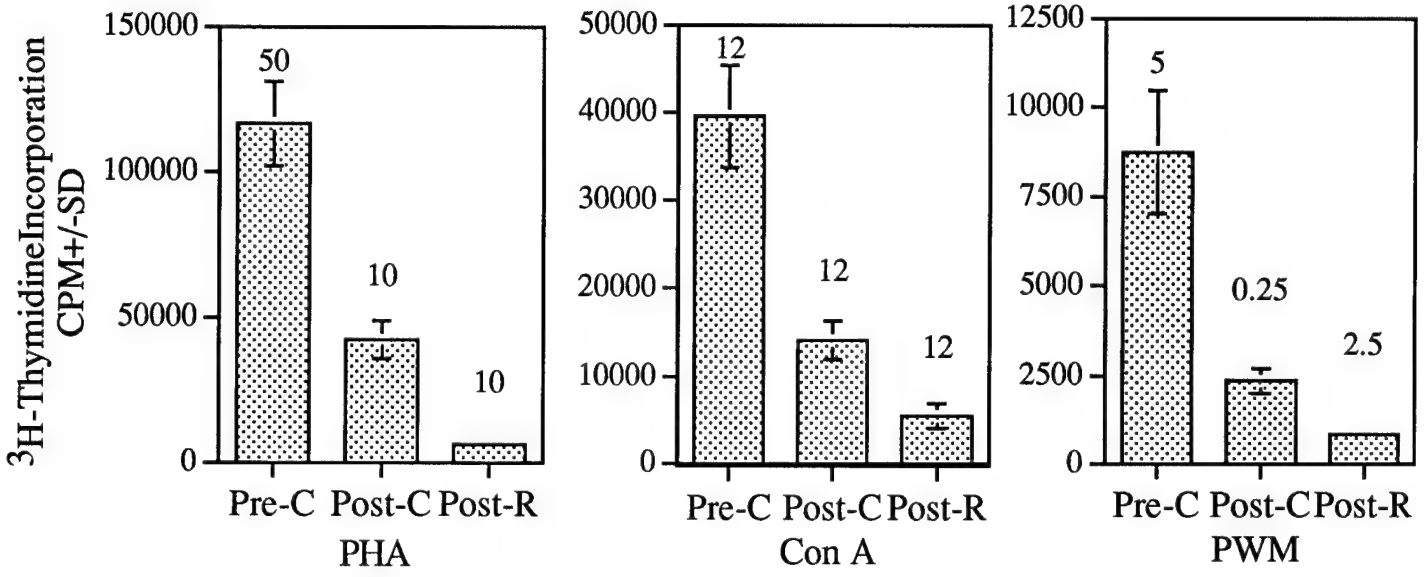
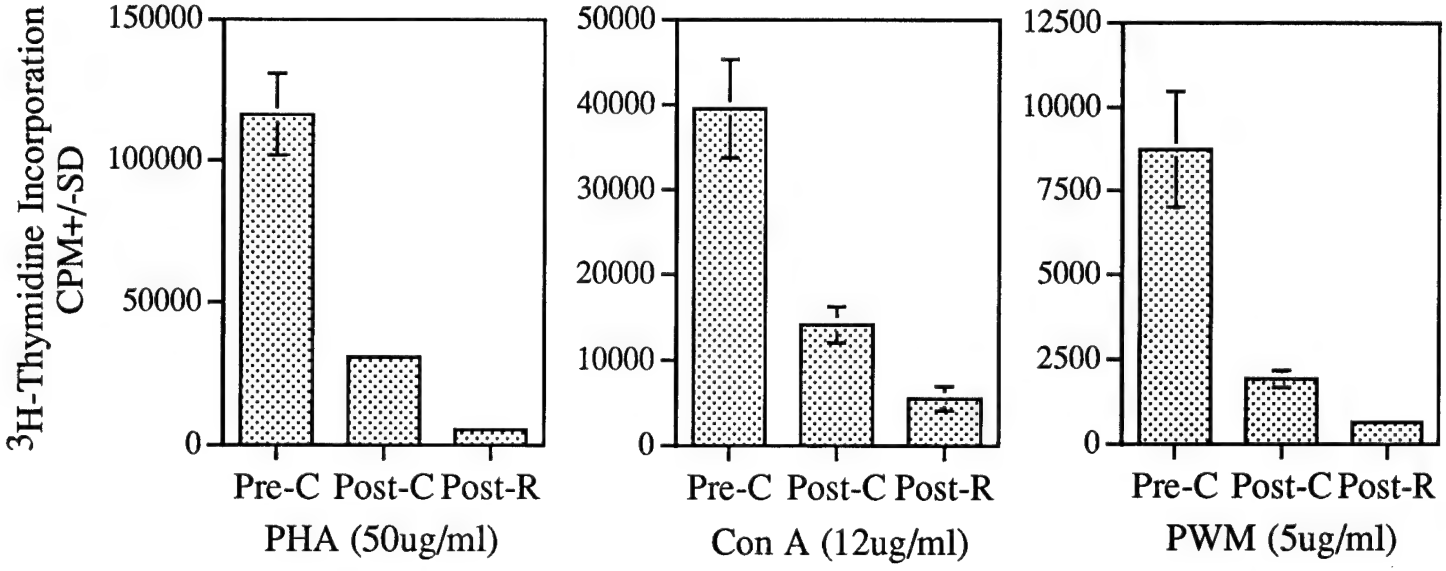
Figure 2: Response to Mitogens, Pre and Post-Chemotherapy.

A. Maximal Response

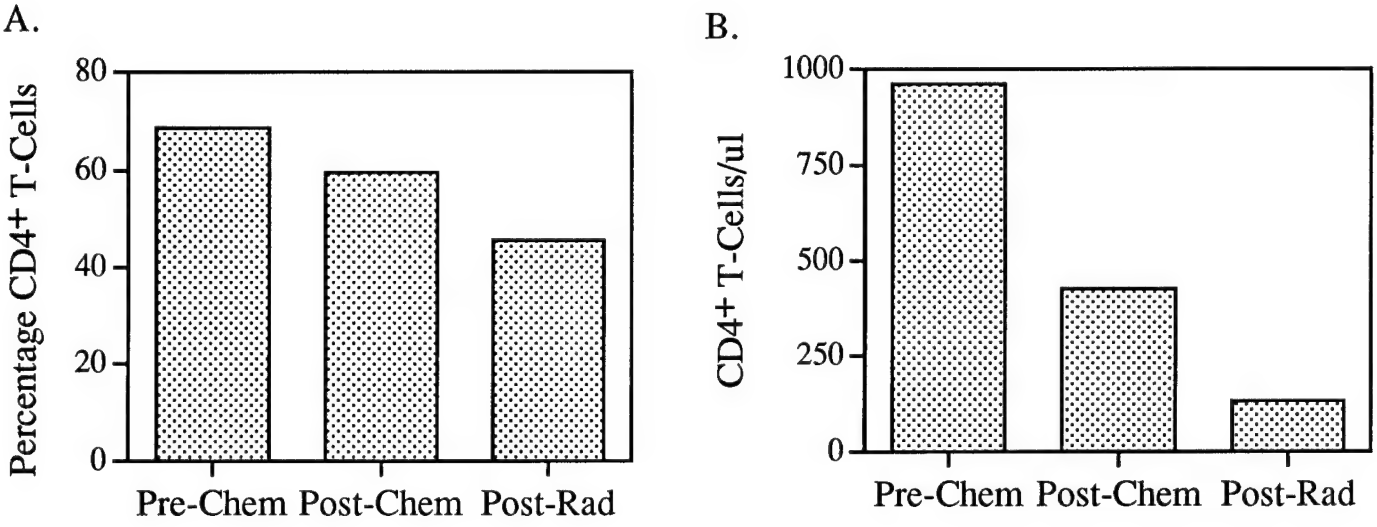


B. Response to one dose



Whole blood mitogen assays were carried out with three different mitogens, PHA, Con A, and PWM at several concentrations: PHA (5, 10, 50ug/ml); Con A (3, 12, 25, and 50ug/ml); and PWM (0.25, 2.5, and 5ug/ml). ^{3}H-Thymidine incorporation was used to indicate cpm in replicate (6) cultures of each. Results were calculated as average CPM+/-SD. Shown are A. maximum incorporation pre-chemotherapy (Pre C), post-chemotherapy (Post C), and post-radiation (Post R). The doses are given above the SD bars. B. incorpotation to a maximal dose of each mitogen.

Figure 3: CD4+ T-Lymphocyte levels following chemotherapy and radiation.



Whole blood phenotyping was carried out with monoclonal antibodies and flow cytometric analysis as described in the test. Shown are the $CD4^+$ T-lymphocytes percentages A and total cells/ul B.
Pre-Chem=pre-chemotherapy; Post-Chem=post-chemotherapy; Post-Rad=post radiation.

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Exercise Protocol

1. Stretching and warm-up: 5-10 minutes

2. Resistance exercise protocol

Week 1: one set of each exercise 60 second rest breaks 10-12 reps
Week 2: two sets of each exercise 60 second rest breaks 8-12 reps
Weeks 3-24: three sets of each exercise 90 second rests after Squats 60 seconds thereafter
8-12 reps

Exercises:

Squats
- Feet shoulder width apart
- Bands go on around knees
- Try to get subject to reach parrallel with the floor
- Head up
- Try to get subjects to come up quickly

Record band color and number of wraps around each foot

Leg extensions
- Subject lies face down
- Figure 8 wrap around foot
- hold band with both hands at the base of the neck
- Full range of motion

Record band color and amount of unused band

Leg curls
- Subject lies face down
- Band over heel
- Spotter holds band
- Full range of motion

Record band color

Calf raises
- Subject stands with front 1/2 of foot on a platform
- Let heels sink then lift themselves to starting position
- One or two feet at a time

Chest Press
- Regular grip
- Both bands below elbows
- Try to keep shoulders elevated
- Return to starting position slowly

Record color and number of wraps

Bicep curl

Stand on band so there is some tension at the start
Hands touching
Return slowly
Keep elbows close to the body

Record color and number of wraps around each hand

Tricep Curl

Exercising arm starts parrallel to the floor
other hand holds band at opposite hip
Start with some tension on the band
Full range of motion
Return slowly

Record color, number of wraps and amount of unused band

Seated row

Hands and feet together
Bands will need to be wrapped around both feet
Start with tension
Full range of motion

Record color and number of wraps around both feet

Upright row

Spread feet apart so there is tension at the start
Hands together
Pull all the way up to the chin

Record color and wraps around feet

Crunches

Two sets of 10-20 depending on the subject

3. Aerobic exercise

15 minutes for weeks 1 and 2. Maintain heart rate at approximately 60% of maximal heart rate

20 minutes for the rest of the program. Weeks 3 and 4 maintain heart rate between 60 and 70% of maximal heart rate.

Weeks 5-24. Maintain heart rate around 75% of maximal heart rate.

4. 5 minute cool down, quiet walking

Name_____ **Sheet number**_____

Weeks 1 and 2

	Week 1					Week 2			
Exercise Heart rate	Date	Date	Date	Date		Date		Date	
Squats									
Leg Ext.									
Leg Curls									
Calf Raises									
Chest Press									
Bicep Curl									
Tricep Curl									
Seated Row									
Upright Row									
Crunch-es									
Aerobics Machine work load Pulse start 5 min 10 min 15 min. end									

Name_____ **Sheet number**_____

Weeks 3 to 24

Exercise	Date	Starting heart rate		Date	Starting heart rate		Date	Starting heart rate	
Squats									
Leg Ext.									
Leg Curls									
Calf Raises									
Chest Press									
Bicep Curl									
Tricep Curl									
Seated Row									
Upright Row									
Crunch-es									
Aerobics machine work load Pulse start 5 min 10 min 15 min end									

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Breast Cancer Exercise Study
Muscle Strength Testing Data Form

Name _____ Test #_____

Group _____

Date _____ Time _____ AM. PM.

Weight _____ kg (in exercise clothes; no shoes)

Height _____(cm)

Kincom Leg Strength

Leg Tested: _____

Scores:

Comments:

Tricep Strength Test

Arm tested: Left or right (circle)

Trial #1 score _____ Trial #2 score _____ Trial #3 score _____

Trial #4 score _____ (if necessary) Trial #5 score _____ (if necessary)

Best score: _____

Grip Strength Test

Grip Slot ____

Right arm #1_____ kg #2 _____kg #3 _____kg:

Best score ____ Newtons (kg X 10)

Left arm #1_____ kg #2 _____kg #3 _____kg

Best score ____ Newtons (kg X 10)

Vertical Jump Test

Weight ____kg

Side tested: left or right (circle)

Standing Reach Position _____ cm

Trial #1 _____cm - Stand height_____ = Jump Height ____ cm

Trial #2_____cm - Stand height_____ = Jump Height ____ cm

Trial #3 _____cm - Stand height_____ = Jump Height ____ cm

Jump Height _____ cm = _____ m

Power ($kg \cdot m \cdot s^{-1}$) = 2.21 x Weight (kg) x $\sqrt{}$ D (m) _____ ($kg \cdot m \cdot s^{-1}$)
Power (Watts) = Power ($kg \cdot m \cdot s^{-1}$) X 10 _____ (Watts)

Formulas:
Power ($kg \cdot m \cdot s^{-1}$) = 2.21 x Weight (kg) x $\sqrt{}$ D (m)

Power ($N \cdot m \cdot s^{-1}$ or Watts) = Power ($kg \cdot m \cdot s^{-1}$) x 10

Bicep 1 RM Strength

Arm Tested: left or right (circle)

Beginning weight ____lbs # reps _____

Weight #2 ____reps Weight #3 ____reps Weight #4 ____ reps

1RM _____ (lbs)

Noll Physiological Research Center & General Clinical Research Center

Date___/___/___
Room # _____

GRADED EXERCISE TEST

Subject:_____ **ID#:**_____ **Height**_____**in.** _____**cm.** **Weight**_____**lbs.** _____**kgs.**
Study_____**Primary Investigator**_____ **Age**_____
Temperature_____'C pH:0_____mmHg
Physician_____**M.D. , D.O.** **Stress Test Leader**_____ **Assistants**_____

Test Indication: _____ **Marquette Protocol:** _____
Test Type: _____ **GXT Protocol:** _____

GRADE (%)																	
SPEED (mph)																	
RESISTANCE (Watts)																	
TIME (min.)																	
HEART RATE (bpm)																	
BLOOD PRESSURE (mmHg)																	
EKG INTERPRETATION																	
R.P.E.																	

RECOVERY

GRADE (%)																	
SPEED (mph)																	
RESISTANCE (Watts)																	
TIME (min.)																	
HEART RATE (bpm)																	
BLOOD PRESSURE (mmHg)																	
EKG INTERPRETATION																	
R.P.E.																	

REASON FOR TERMINATION:

Comments/Impressions:

Max. HR:
Max. B.P:
Max. Workoad:

ACSM Predicted VO2:
Measured V02:

Gas Analysis on Reverse

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NAME_____
DATE_____

FUNCTIONAL ASSESSMENT OF CANCER THERAPY-ANEMIA (FACT An) QUESTIONNAIRE

By:

S.B. Yellen, D.F. Cella, K. Webster, C. Blendowski, and E. Kaplan. 1997. Measuring Fatigue and Other Anemia-Related Symptoms with the Functional Assessment of Cancer Therapy (FACT) Measurement System. J. Pain and Symptom Management 13:63-73.

Functional Assessment of Cancer Therapy–Anemia (FACT-An) (Version 3)

Below is a list of statements that other people with your illness have said are important. By circling one number per line, please indicate how true each statement has been for you *during the past 7 days*.

	Not at all	A little bit	Some-what	Quite a bit	Very much
PHYSICAL WELL-BEING					
1. I have a lack of energy	0	1	2	3	4
2. I have nausea	0	1	2	3	4
3. Because of my physical condition, I have trouble meeting the needs of my family	0	1	2	3	4
4. I have pain	0	1	2	3	4
5. I am bothered by side effects of treatment	0	1	2	3	4
6. I feel sick	0	1	2	3	4
7. I am forced to spend time in bed	0	1	2	3	4
8. Looking at the above 7 questions, how much would you say your PHYSICAL WELL-BEING affects your quality of life? (circle one)	0 1 2 3 4 5 6 7 8 9 10 Not at all — Very much so				
SOCIAL/FAMILY WELL-BEING					
9. I feel distant from my friends	0	1	2	3	4
10. I get emotional support from my family	0	1	2	3	4
11. I get support from my friends and neighbors	0	1	2	3	4
12. My family has accepted my illness	0	1	2	3	4
13. Family communication about my illness is poor	0	1	2	3	4
14. I feel close to my partner (or the person who is my main support)	0	1	2	3	4
15. Have you been sexually active during the past year? Y/N If yes: I am satisfied with my sex life	0	1	2	3	4
16. Looking at the above 7 questions, how much would you say your SOCIAL/FAMILY WELL-BEING affects your quality of life? (circle one)	0 1 2 3 4 5 6 7 8 9 10 Not at all — Very much so				
RELATIONSHIP WITH DOCTOR					
17. I have confidence in my doctor(s)	0	1	2	3	4
18. My doctor is available to answer my questions	0	1	2	3	4
19. Looking at the above 2 questions, how much would you say your RELATIONSHIP WITH THE DOCTOR affects your quality of life? (circle one)	0 1 2 3 4 5 6 7 8 9 10 Not at all — Very much so				
EMOTIONAL WELL-BEING					
20. I feel sad	0	1	2	3	4
21. I am proud of how I'm coping with my illness	0	1	2	3	4
22. I am losing hope in the fight against my illness	0	1	2	3	4
23. I feel nervous	0	1	2	3	4
24. I worry about dying	0	1	2	3	4
25. I worry that my condition will get worse	0	1	2	3	4
26. Looking at the above 6 questions, how much would you say your EMOTIONAL WELL-BEING affects your quality of life? (circle one)	0 1 2 3 4 5 6 7 8 9 10 Not at all — Very much so				

	Not at all	A little bit	Some-what	Quite a bit	Very much
FUNCTIONAL WELL-BEING					
27. I am able to work (include work in home)	0	1	2	3	4
28. My work (include work in home) is fulfilling	0	1	2	3	4
29. I am able to enjoy life	0	1	2	3	4
30. I have accepted my illness	0	1	2	3	4
31. I am sleeping well	0	1	2	3	4
32. I am enjoying the things I usually do for fun	0	1	2	3	4
33. I am content with the quality of my life right now	0	1	2	3	4
34. Looking at the above 7 questions, how much would you say your FUNCTIONAL WELL-BEING affects your quality of life? (circle one)	0 1 2 3 4 5 6 7 8 9 10 Not at all				Very much so
ADDITIONAL CONCERNS					
*35. I feel fatigued	0	1	2	3	4
*36. I feel weak all over	0	1	2	3	4
*37. I feel listless ("washed out")	0	1	2	3	4
*38. I feel tired	0	1	2	3	4
*39. I have trouble starting things because I am tired	0	1	2	3	4
*40. I have trouble finishing things because I am tired	0	1	2	3	4
*41. I have energy	0	1	2	3	4
42. I have trouble walking	0	1	2	3	4
*43. I am able to do my usual activities	0	1	2	3	4
*44. I need to sleep during the day	0	1	2	3	4
45. I feel lightheaded (dizzy)	0	1	2	3	4
46. I get headaches	0	1	2	3	4
47. I have been short of breath	0	1	2	3	4
48. I have pain in my chest	0	1	2	3	4
*49. I am too tired to eat	0	1	2	3	4
50. I am interested in sex	0	1	2	3	4
51. I am motivated to do my usual activities	0	1	2	3	4
*52. I need help doing my usual activities	0	1	2	3	4
*53. I am frustrated by being too tired to do the things I want to do	0	1	2	3	4
*54. I have to limit my social activity because I am tired	0	1	2	3	4
55. Looking at the above 20 questions, how much would you say these ADDITIONAL CONCERNS affect your quality of life? (circle one)	0 1 2 3 4 5 6 7 8 9 10 Not at all				Very much so

* These items comprise the 13-item fatigue subscale.

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YOUR DIET REPORT

Study #: _____
Name/ ID#: _____
Age: _____
Date: _____

Study Period: Pre-chemo ___
Post-chemo ___
Post-radiation ___
Pre-exercise ___
Exercise 1 ___
Exercise 2 ___

Please tell us about your diet, supplements, and medications during this <u>past week</u> (the last 7 days). Your report is divided into 3 sections:

Section 1. Foods and Beverages

Section 2. Vitamin, Mineral, and Herbal Supplements

Section 3. Medications

Please fill out each section carefully. Choose only <u>1 response</u> for each item.

Please return this report to: _____

_____

Please return by this date: _____

If you have questions, contact: _____

_____

Section 1. Foods and Beverages

- This section includes 9 lists of foods and beverages. Please look at these before you begin.

Breads, cereals, and grain products	Beverages
Fruits and juices	Protein foods
Fats and oils	Desserts and sweets
Milk, yogurt, and cheeses	Miscellaneous foods *(fast foods, soups,*
Vegetables	*snack foods, condiments, etc.)*

- Tell us how often you consumed each food and beverage this past week (the last 7 days). Please give only 1 response for each item.

- If you ate a food every day, fill in the daily column. If you ate it less than once a day, fill in the weekly column.

  Example: If you ate 2 apples every day, write 2 under the daily column.
  If you ate 2 apples this week, write 2 under the weekly column.

- Try to choose the best match for each item, even if the foods or beverages you consumed don't always exactly match the item listed.

- Look at the serving sizes listed for each item. Compare the amount you consumed to the serving size listed. Write how much you consumed in terms of the serving size listed.

  Example: The serving size listed for a bagel is 1/2 of a bagel.
  If you ate 1 bagel this week, write 2 servings in the weekly column.
  If you ate 2 bagels this week, write 4 servings in the weekly column.

- Fractions can't be used, so round off the servings to the nearest whole number.

- For meats, poultry, and fish, 3 ounces is the size of a deck of cards or an audiocassette tape.

- Many foods are actually a combination of several food items. You will find some of these foods (pizza, hamburgers, and burritos) in the "Miscellaneous Foods" section. Other combination foods (such as casseroles, sandwiches, and chili) are not listed in the report. If you ate these kinds of foods, write the separate items that made up the food.

  Example: If you ate 1 turkey sandwich this week (3 oz. turkey + 1 Tbsp. mayonnaise on a bagel), you would write it this way:

Food Name/ Description	Serving Size	Number of servings this week	
		Daily	Weekly
Poultry: chicken, turkey, duck	3 ounces	1	
English muffin, bagel, pita bread	1/2 item	2	
Mayonnaise	1 Tbsp.	1	

A. Breads, Cereals, and Grain Products

Food Name/ Description	Serving Size	Number of servings this week	
		Daily	Weekly
Whole grain breads (whole-wheat, rye, pumpernickel)	1 slice		
White breads: hamburger or hot dog bun (1/2 item); sliced bread (1 slice); low calorie breads (2 slices), etc.	1 serving		
English muffin, bagel, pita bread	1/2 item		
Whole grain crackers: Triscuits, Wheat Thins (4-6 each), etc.	1 serving		
Other crackers: Saltines, Ritz (4-6 each), etc.	1 serving		
Tortilla, corn, 6" diameter (medium)	1 item		
Muffins	1 item		
Pancakes (2) or waffles (1-7" diameter)	1 serving		
Whole grain hot cereal: rolled oats, Roman Meal, etc.	1/2 cup		
Instant hot cereal: cream of wheat, cream of rice, etc.	1/2 cup		
Cold cereals (fiber/grain): shredded wheat, bran flakes, etc.	3/4 cup		
Cold cereals (added sugar): Frosted Flakes, Sugar Smacks, Rice Krispies, etc.	3/4 cup		
Rice, cooked	1/2 cup		
Pasta, cooked	1/2 cup		
OTHER *(please specify):*			
OTHER *(please specify):*			

B. Fruits and Juices

Food Name/ Description	Serving Size	Number of servings this week	
		Daily	Weekly
Apple or pear, fresh, medium	1 item		
Banana, medium	1 item		
Orange (1 item) or grapefruit (1/2 item)	1 serving		
Peach (1 item), nectarine (1/2 item), apricot (2 items)	1 serving		
Berries	3/4 cup		
Cantaloupe, medium	1/4 item		
Other melon: watermelon, honeydew, casaba	1 cup		
Pineapple, fresh	1/2 cup		
Dried fruits: raisins (2 Tbsp.), dates (2 items), prunes (2 items), dried apricots (4 items), etc.	1 serving		
Canned or frozen fruit	1/2 cup		
Orange juice or grapefruit juice	1/2 cup		
Tomato juice or vegetable juice	1/2 cup		
Other juices: apple, grape, pineapple, or cranberry, etc.	1/2 cup		
Fruit drinks: lemonade, punch, Koolaid	1/2 cup		
OTHER *(please specify):*			
OTHER *(please specify):*			

C. Fats and Oils

Food Name/ Description	Serving Size	Number of servings this week	
		Daily	Weekly
Vegetable oils: corn, safflower, soy, etc.	1 Tbsp.		
Olive oil	1 Tbsp.		
Vegetable shortenings	1 Tbsp.		
Lard	1 Tbsp.		
Margarine	1 tsp.		
Butter	1 tsp.		
Mayonnaise	1 Tbsp.		
Regular salad dressing	1 Tbsp.		
Low calorie salad dressing	1 Tbsp.		
Sour cream	1 Tbsp.		
Cream cheese	1 Tbsp.		
Half & half, table cream	1 Tbsp.		
OTHER *(please specify):*			
OTHER *(please specify):*			

D. Milk, Yogurt and Cheeses

Food Name/ Description	Serving Size	Number of servings this week	
		Daily	Weekly
Skim milk, low fat milk (white or chocolate)	1 cup (8 fl. oz.)		
Whole milk, white	1 cup (8 fl. oz.)		
Whole milk, chocolate	1 cup (8 fl. oz.)		
Yogurt	1 cup (8 oz.)		
Cheese (hard): cheddar, colby, American, Monterey jack, etc.	1 ounce		
Cheese (soft-medium): Swiss, mozzarella, ricotta, string, etc.	1 ounce		
Cottage cheese	1/2 cup		
OTHER *(please specify):*			
OTHER *(please specify):*			

E. Vegetables

Food Name/ Description	Serving Size	Number of servings this week	
		Daily	Weekly
Salads: lettuce, celery, green pepper, onion, etc.	1 cup		
Dark green leafy vegetables, raw or cooked: spinach, kale, collard greens, etc.	1/2 cup		
Carrots, raw or cooked	1/2 cup		
Tomato, fresh, medium	1 item		
Starchy vegetables, cooked: corn, peas, mixed vegetables	1/2 cup		
Other vegetables, cooked: green beans, beets, zucchini, etc.	1/2 cup		
Cauliflower, broccoli, Brussels sprouts, cabbage, etc.	1/2 cup		
Winter squash, cooked: acorn, butternut, hubbard, etc.	1/2 cup		
White potato, baked, boiled, or mashed	1 item		
Sweet potatoes or yams, cooked	1/2 cup		
OTHER *(please specify):*			
OTHER *(please specify):*			

F. Beverages

Food Name/ Description	Serving Size	Number of servings this week	
		Daily	Weekly
Cola drinks	1 can (12 fl. oz.)		
Diet cola drinks	1 can (12 fl. oz.)		
Non-cola drinks: 7-up, Sprite, Slice, etc.	1 can (12 fl. oz.)		
Diet non-cola drinks	1 can (12 fl. oz.)		
Coffee or tea	1 can (8 fl. oz.)		
Coffee or tea, decaffeinated	1 can (8 fl. oz.)		
Hot chocolate or cocoa	1 can (8 fl. oz.)		
Beer	1 can (12 fl. oz.)		
Wine, dry or table (red, white, blush)	1 glass (4 fl. oz.)		
Liquor: vodka, whiskey, gin, rum, etc.	1 shot (2 fl. oz.)		
Water: tap water (from municipal water supply)	1 glass (8 fl. oz.)		
Water: bottled (plain or seltzer, no calories)	1 glass (8 fl. oz.)		
OTHER *(please specify):*			
OTHER *(please specify):*			

G. Protein Foods

Food Name/ Description	Serving Size	Number of servings this week	
		Daily	Weekly
Legumes, cooked: lentils, pinto beans, navy beans	1 cup		
Nuts & seeds: peanuts, almonds, sunflower seeds	1/4 cup		
Peanut butter, nut butters	1 Tbsp.		
Tofu or other meat substitutes	3 ounces		
Beef: rib roast, steak, pot roast, veal, etc.	3 ounces		
Beef, ground, cooked	3 ounces		
Pork: chops, roast, ham	3 ounces		
Lamb: chops, roast	3 ounces		
Poultry: chicken, turkey, duck	3 ounces		
Fish, canned with oil: tuna, sardines	3 ounces		
Fish, tuna, water pack	3 ounces		
Fish, fresh or frozen, (no breading): trout, halibut, sole, etc.	3 ounces		
Shellfish: shrimp, scallops, lobster, clams, etc.	3 ounces		
Eggs, whole, large	1 item		
Egg substitutes or egg whites	1/4 cup		
Lunch meats: bologna, salami, etc.	1 ounce		
Frankfurters or sausage link (4" x 1")	1 item		
OTHER *(please specify):*			
OTHER *(please specify):*			

H. Desserts and Sweets

Food Name/ Description	Serving Size	Number of servings this week	
		Daily	Weekly
Cookies: chocolate chip, oatmeal, peanut butter, etc.	2 items		
Brownies, 2"x 2"	1 item		
Doughnut or sweet roll	1 item		
Cake (1/12 of a 9 inch cake)	1 slice		
Granola bar (1 item) or granola (1/2 cup)	1 serving		
Pie (1/8 of a whole pie)	1 slice		
Gelatin, flavored	1/2 cup		
Pudding or custard	1/2 cup		
Ice cream	1/2 cup		
Ice milk	1/2 cup		
Sherbet	1/2 cup		
Candy bar, chocolate bar (1 bar), M&Ms (1 pkg.)	1 item		
Hard candy, gum drops, Lifesavers	1 item		
OTHER *(please specify):*			
OTHER *(please specify):*			

I. Miscellaneous Foods

Food Name/ Description	Serving Size	Number of servings this week	
		Daily	Weekly
Fast food: pizza	1 slice		
Fast food: hamburger or cheeseburger	1 item		
Fast food: burrito or taco	1 item		
Bacon	2 slices		
Popcorn, popped	2 cups		
Chips: potato, corn, tortilla (10 to 15 pieces)	1 ounce		
Catsup or chili sauce	1 Tbsp.		
Tomato based sauce (spaghetti sauce)	1/2 cup		
Pickles (1 slice) or pickle relish (1 Tbsp.)	1 serving		
Olive	5 items		
Avocado (1/8 item)	1/8 item		
Sauces: soy sauce, steak sauce, barbecue sauce	1 Tbsp.		
Brown gravy, giblet gravy, white sauce	1/4 cup		
Soups, vegetable or noodle type	1 cup		
Soups, cream	1 cup		
Chewing gum	1 piece		
Sugar, honey, jam, jelly, syrups	1 Tbsp.		
OTHER *(please specify):*			
OTHER *(please specify):*			

Section 2. Vitamin, Mineral, and Herbal Supplements

(Please also include name and dosage of all vitamins, minerals and herbs not listed below)

Name/ Description	Dosage	Number of times this week	
		Daily	Weekly
Multivitamin & mineral			
Multivitamin			
Multimineral			
Vitamin A			
Vitamin B12			
Vitamin C			
Vitamin D			
Vitamin E			
Calcium with Vitamin D			
Calcium			
Folic acid			
Iron			
Magnesium			
Potassium			
Selenium			
Zinc			
OTHER *(please specify):*			

Section 3. Medications

(Please list name and dosage of all over-the-counter and prescription medications not listed below)

Name/ Description	Dosage	Number of times this week	
		Daily	Weekly
Over the counter drugs *(please specify):*			
Prescription drugs *(please specify)*:			

Mastro
DAMD17-98-1-8142

Your Physical Activity Report

Study # _____
Name/ID# _____
Age _____
Date _____

Study Period:

- Pre-chemo ___
- Post-chemo ___
- Post-radiation___
- Pre-exercise ___
- Exercise 1 ___
- Exercise 2 ___

Please fill out this physical activity questionnaire according to your physical activity during the past week (7 days).

Please return this report to _____

Please return by this date _____

If you have any questions please contact Dr. Nancy Williams at 865-1346(phone) or niw1@psu.edu **(email).**

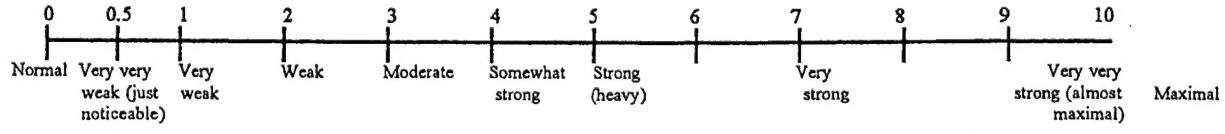
Thanks for your participation.

Paffenbarger Physical Activity Questionnaire

1. How many city blocks or their equivalent do you normally walk each day? _____ blocks/day (Let 12 blocks = 1 mile)
2. What is your usual pace of walking? (Please check one.)
   a. ___ Casual or strolling (less than 2 mph) b. ___ Average or normal (2 to 3 mph)
   c. ___ Fairly brisk (3 to 4 mph) d. ___ Brisk or striding (4 mph or faster)
3. How many flights or stairs to you climb up each day? ___ flights/day (Let 1 flight = 10 steps.)
4. List any sports or recreation you have actively participated in during the past Week. Please remember seasonal sports or events.

Sport, Recreation, or Other Physical Activity	Number of Times/Week	Average Time/Episode: Hours	Average Time/Episode: Minutes	Years Participation
a.				
b.				
c.				
d.				
e.				
f.				

5. Which of these statements best expresses your view? (Please check one.)
   a. ___ I take enough exercise to keep healthy. b. ___ I ought to take more exercise. c. ___ Don't know
6. At least once a week, do you engage in regular activity akin to brisk walking, jogging, bicycling, swimming, etc. long enough to work up a sweat, get your heart thumping, or get out of breath?
   ___ No Why not? _____ ___ Yes How many times per week? ___ Activity:_____
7. When you are exercising in your usual fashion, how would you rate your level of exertion (degree of effort)? (Please circle one number.)



8. On a usual weekday and a weekend day, how much time do you spend on the following activities? Total for each day should add to 24 hours.

	Usual Weekday Hours/Day	Usual Weekend Day Hours/Day
a. Vigorous activity (digging in the garden, strenuous sports, jogging, aerobic dancing, sustained swimming, brisk walking, heavy carpentry, bicycling on hills, etc.)		
b. Moderate activity (housework, light sports, regular walking, golf, yard work, lawn mowing, painting, repairing, light carpentry, ballroom dancing, bicycling on level ground, etc.)		
c. Light activity (office work, driving car, strolling, personal care, standing with little motion, etc.)		
d. Sitting activity (eating, reading, desk work, watching TV, listening to radio, etc.)		
e. Sleeping or reclining		